



Source details

EurAsian Journal of BioSciences

Scopus coverage years: from 2013 to 2020

Publisher: Foundation for Environmental Protection and Research

ISSN: 1307-9867

Subject area: [Agricultural and Biological Sciences: General Agricultural and Biological Sciences](#)

[Environmental Science: General Environmental Science](#) [View all](#)

Source type: Journal

CiteScore 2020

0.6



SJR 2020

0.157



SNIP 2020

0.625



[View all documents](#) >

[Set document alert](#)

[Save to source list](#)

[CiteScore](#) [CiteScore rank & trend](#) [Scopus content coverage](#)

i Improved CiteScore methodology

CiteScore 2020 counts the citations received in 2017-2020 to articles, reviews, conference papers, book chapters and data papers published in 2017-2020, and divides this by the number of publications published in 2017-2020. [Learn more](#) >

CiteScore ~~2020~~

$$0.6 = \frac{503 \text{ Citations 2017 - 2020}}{813 \text{ Documents 2017 - 2020}}$$

Calculated on 05 May, 2021

CiteScoreTracker 2021

$$1.1 = \frac{915 \text{ Citations to date}}{801 \text{ Documents to date}}$$

Last updated on 05 January, 2022 - Updated monthly

CiteScore rank 2020

Category	Rank	Percentile
Agricultural and Biological Sciences	#158/209	24th
— General Agricultural and Biological Sciences		
Environmental Science	#171/220	22nd
— General Environmental Science		

[View CiteScore methodology](#) > [CiteScore FAQ](#) > [Add CiteScore to your site](#)

About Scopus

[What is Scopus](#)
[Content coverage](#)
[Scopus blog](#)
[Scopus API](#)
[Privacy matters](#)

Language

[日本語に切り替える](#)
[切换到简体中文](#)
[切换到繁體中文](#)
[Русский язык](#)

Customer Service

[Help](#)
[Contact us](#)

ELSEVIER

[Terms and conditions](#) ↗ [Privacy policy](#) ↗

Copyright © Elsevier B.V. ↗. All rights reserved. Scopus® is a registered trademark of Elsevier B.V.

We use cookies to help provide and enhance our service and tailor content. By continuing, you agree to the use of cookies.

 RELX



Submit Your Manuscript With Us

Learn More About How to Publish and our Partnership with Hindawi.

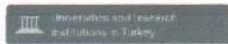
Hindawi

Open

EurAsian Journal of BioSciences

COUNTRY

Turkey



SUBJECT AREA AND CATEGORY

- Agricultural and Biological Sciences
 - Agricultural and Biological Sciences (miscellaneous)
- Biochemistry, Genetics and Molecular Biology
 - Biochemistry, Genetics and Molecular Biology (miscellaneous)
- Environmental Science
 - Environmental Science (miscellaneous)

PUBLISHER

Foundation for Environmental Protection and Research

Submit Your Manuscript With Us



Open

H-INDEX

11

PUBLICATION TYPE

Journals

ISSN

13079867

COVERAGE

2013-2020

INFORMATION

- Homepage
- How to publish in this journal
- ejbios@ejbios.org



Prepare Your Manuscript

Trusted by the most respected names in scientific publishing.

Open





AJE: English Editing & Author Services for Research Publication

American Journal Experts

Open

SCOPE

EurAsian Journal of BioSciences (Abbrev. Eurasia J Biosci or EJOBIO) is an international refereed electronic journal. It publishes the results of original research in the field of biological sciences restricted to morphology, physiology, genetics, taxonomy, ecology and biogeography of both prokaryotic and eucaryotic organisms. The journal encourages submission of manuscripts dealing with plant biology, animal biology, plant physiology, microbiology, hydrobiology, ecology and environmental science, ethnobiology, biodiversity and conservation biology. EurAsian Journal of BioSciences publishes original articles in the following areas: -Agriculture, Fisheries & Food -Anatomy & Morphology -Behavioural Sciences -Biology, Biochemistry and Biotechnology -Biophysics -Biology Education -Cellular Biology and Anatomical Sciences -Ecology, Evolution & Environment -Entomology -Forestry -General Biology -Genetics & Heredity -Life Sciences - Other topics -Microbiology and Immunology -Molecular Biology -Mycology -Palaeontology -Parasitology -Pharmacology & Pharmacy -Physiology and Related Sciences -Plant Sciences -Toxicology -Veterinary Sciences -Virology -Zoology

Join the conversation about this journal

Quartiles



AJE: English Editing & Author Services for Research Publication

American Journal Experts

Open

FIND SIMILAR JOURNALS

- | | | | | |
|--|---|---|---|--|
| 1
Bioscience Research
QAK
35%
similarity | 2
Plant Archives
INF
34%
similarity | 3
Pertanika Journal of Tropical Agricultural Science
MVE
33%
similarity | 4
Saudi Journal of Biological Sciences
SAJ
32%
similarity | 5
Proceedings of the National Academy of Sciences India
IND
32%
similarity |
|--|---|---|---|--|



EurAsian Journal of BioSciences

Q4 Agricultural and Biological Sciences (Interdisciplinary) - 2020

SJR 2020: 0.16

powered by scimagojr.com

Show this widget in your own website

Just copy the code below and paste within your html code:

`<a href="https://www.scim..."`

SCImago Graphica

Explore, visually communicate and make sense of data with our new free tool.

[Get it](#)

AJE: English Editing & Author Services for Research Publication

American Journal Experts

[Open](#)

Metrics based on Scopus® data as of April 2021

M **Mariam Alla Tuma** 6 months ago

Good day
 may I know how long time from submitting a paper to get an acceptance letter? and how much the publication fee? Can you tell me if this journal (EurAsian Journal of BioSciences) was in Scopus or not.
 Thanks

[reply](#)

Melanie Ortiz 5 months ago SCImago Team

Dear Mariam,
 Thank you for contacting us.
 We are sorry to tell you that SCImago Journal & Country Rank is not a journal. SJR is a portal with scientometric indicators of journals indexed in Elsevier/Scopus. We suggest you consult the Scopus database directly to see the current index status as SJR is a static image of Scopus, which is changing every day. For further information about this journal, please visit the journal's website or contact directly with the editorial staff.
 Best Regards, SCImago Team

M **Mutaz** 9 months ago

Dears

2020, Volume 14, Issue 2 (Volume 14, Issue 2, August-December 2020)

[The distribution of lethal Holstein haplotypes affecting female fertility among the Russian Black-and-White cattle \(/article/the-distribution-of-lethal-holstein-haplotypes-affecting-female-fertility-among-the-russian-7818\)](#)

Abdulrahman Khatib, Alexander M. Mazur, Egor Prokhorchouk

[Download Full Article - PDF format \(/download/the-distribution-of-lethal-holstein-haplotypes-affecting-female-fertility-among-the-russian-7818.pdf\)](#)

Abstract

[Microbial study of Trichophyton rubrum isolated from various Tinea infections \(/article/microbial-study-of-trichophyton-rubrum-isolated-from-various-tinea-infections-7819\)](#)

Raed Ali Hussain Shabaa

[Download Full Article - PDF format \(/download/microbial-study-of-trichophyton-rubrum-isolated-from-various-tinea-infections-7819.pdf\)](#)

Abstract

[The association between genetic polymorphisms of IL-6 gene and susceptibility of systemic lupus erythematosus in Iraqi population \(/article/the-association-between-genetic-polymorphisms-of-il-6-gene-and-susceptibility-of-systemic-lupus-7820\)](#)

Rand Muhammed Abdul-Hussein Al-Hussein

[Download Full Article - PDF format \(/download/the-association-between-genetic-polymorphisms-of-il-6-gene-and-susceptibility-of-systemic-lupus-7820.pdf\)](#)

Abstract

[Some questions about Teae folia \(Thea sinensis L. seu Camellia sinensis L. Kuntze\) as a medicinal raw material \(/article/some-questions-about-teae-folia-thea-sinensis-l-seu-camellia-sinensis-l-kuntze-as-medicinal-raw-7821\)](#)

Olena V. Grechana, Anatoly G. Serbin, Sergiy D. Trshchinskiy, Olexandr I. Panasenko, Lina Yu. Klimenko, Tetyana V. Oproshanska, Olena O. Saliy

[Download Full Article - PDF format \(/download/some-questions-about-teae-folia-thea-sinensis-l-seu-camellia-sinensis-l-kuntze-as-medicinal-raw-7821.pdf\)](#)

Abstract

[Study the relationship between Interleukin-35 and clusterin with Mda, Gsh, Cat and Sod among male Iraqi chronic Hepatitis C patients \(/article/study-the-relationship-between-interleukin-35-and-clusterin-with-mda-gsh-cat-and-sod-among-male-7822\)](#)

Shakir F. T. Alaaraji, Shakir M. S. Alfahdawi, Majid A. Mohaisen

[Download Full Article - PDF format \(/download/study-the-relationship-between-interleukin-35-and-clusterin-with-mda-gsh-cat-and-sod-among-male-7822.pdf\)](#)

Abstract

[A survey study for aborted women toward cytomegalovirus and toxoplasma in Babylon City \(/article/a-survey-study-for-aborted-women-toward-cytomegalovirus-and-toxoplasma-in-babylon-city-7823\)](#)

Ashwaq M. S. Al-Jbouri, Nagham Adil Ghani Chabuck, Rasha Fadhel Obaid, Samah Ahmed Kadhum Al-Jebory

[Download Full Article - PDF format \(/download/a-survey-study-for-aborted-women-toward-cytomegalovirus-and-toxoplasma-in-babylon-city-7823.pdf\)](#)

Abstract

[Environmental monitoring plan for marine ports, case study Shuwaikh Port, Kuwait \(/article/environmental-monitoring-plan-for-marine-ports-case-study-shuwaikh-port-kuwait-7824\)](#)

Ahmed Al Rashed, Hossam Mostgab, Ahmed Gad

[Download Full Article - PDF format \(/download/environmental-monitoring-plan-for-marine-ports-case-study-shuwaikh-port-kuwait-7824.pdf\)](#)

Abstract

[The association between plasma and follicular fluid folate levels and the pregnancy rate in women enrolled in ICSI cycles \(/article/the-association-between-plasma-and-follicular-fluid-folate-levels-and-the-pregnancy-rate-in-women-7825\)](#)

Wasan Adnan Abdulhameed, Nahlah Abdulmajeed Hasan, Ali Ibrahim Rahim, A. H. Mohammed

[Download Full Article - PDF format \(/download/the-association-between-plasma-and-follicular-fluid-folate-levels-and-the-pregnancy-rate-in-women-7825.pdf\)](#)

Abstract

[Evaluation of oxidative stress and growth status in molecular diagnostic patients with entamoeba histolytica \(/article/evaluation-of-oxidative-stress-and-growth-status-in-molecular-diagnostic-patients-with-entamoeba-7826\)](#)

Rasha Amer Nouri Al-Tufaili, Rasha Shakir Nima

[Download Full Article - PDF format \(/download/evaluation-of-oxidative-stress-and-growth-status-in-molecular-diagnostic-patients-with-entamoeba-7826.pdf\)](#)

Abstract

[Investigation of cytokines and herpes simplex virus in recurrent abortion in pregnant women \(/article/investigation-of-cytokines-and-herpes-simplex-virus-in-recurrent-abortion-in-pregnant-women-7827\)](#)

Hashem Mohammed Hashem AL-Aaraje, Huda Jameel Baker AL-Khilkhali

[Download Full Article - PDF format \(/download/investigation-of-cytokines-and-herpes-simplex-virus-in-recurrent-abortion-in-pregnant-women-7827.pdf\)](#)

Abstract

[Antibiotic susceptibility and biofilm formation of Lactobacilli spp. isolated from healthy and infected women with bacterial vaginosis \(/article/antibiotic-susceptibility-and-biofilm-formation-of-lactobacilli-spp-isolated-from-healthy-and-7828\)](#)

Zeena Adnan Shalash, Farah Tariq Abdul-Ridha

[Download Full Article - PDF format \(/download/antibiotic-susceptibility-and-biofilm-formation-of-lactobacilli-spp-isolated-from-healthy-and-7828.pdf\)](#)

Abstract

[Heat resistance of introduced apple-tree varieties due to water status and seasonal development under arid conditions Of Mangistau \(/article/heat-resistance-of-introduced-apple-tree-varieties-due-to-water-status-and-seasonal-development-7829\)](#)

O.N. Kossareva, D.N. Zharassova, N.A. Tolep

[Download Full Article - PDF format \(/download/heat-resistance-of-introduced-apple-tree-varieties-due-to-water-status-and-seasonal-development-7829.pdf\)](#)

Abstract

[IL-23/IL-17 axis and disease activity in systemic lupus erythematosus patients \(/article/il-23-il-17-axis-and-disease-activity-in-systemic-lupus-erythematosus-patients-7830\)](#)

Tri Yanti, Yuliasih, Lita Diah Rahmawati

[Download Full Article - PDF format \(/download/il-23-il-17-axis-and-disease-activity-in-systemic-lupus-erythematosus-patients-7830.pdf\)](#)

Abstract

[Factors affecting potential overpayment claim of government health insurance in naval hospital \(/article/factors-affecting-potential-overpayment-claim-of-government-health-insurance-in-naval-hospital-7831\)](#)

Ahmad Samsulhadi, Djazuly Chalidyanto

[Download Full Article - PDF format \(/download/factors-affecting-potential-overpayment-claim-of-government-health-insurance-in-naval-hospital-7831.pdf\)](#)

Abstract

[Factors affecting the occurrence of low birth weight \(/article/factors-affecting-the-occurrence-of-low-birth-weight-7832\)](#)

Sesotianingsih Madiyaning Utami, Ratna Dwi Wulandari

[Download Full Article - PDF format \(/download/factors-affecting-the-occurrence-of-low-birth-weight-7832.pdf\)](#) Abstract[The relationship of nurse characteristics with prevention behavior and control of pulmonary tuberculosis infection \(/article/the-relationship-of-nurse-characteristics-with-prevention-behavior-and-control-of-pulmonary-7833\)](#)

Tintin Sukartini, Ahmad Eko Wibowo, Abu Bakar

[Download Full Article - PDF format \(/download/the-relationship-of-nurse-characteristics-with-prevention-behavior-and-control-of-pulmonary-7833.pdf\)](#)

Abstract

[Factors associated with student snacking consumption \(/article/factors-](#)

[associated-with-student-snacking-consumption-7834](#)

Oktavina Batubara, Yuni Sufyanti Arief, Ilya Krisnana

[Download Full Article - PDF format \(/download/factors-associated-with-student-snacking-consumption-7834.pdf\)](#) Abstract[Relationship between attitude, motivation, and workload with officers' performance of finding leprosy patients early \(/article/relationship-between-attitude-motivation-and-workload-with-officers-performance-of-finding-leprosy-7835\)](#)

Riana Dwi Setyantari, Ernawaty, Yeni Rahmah Husniyawati

[Download Full Article - PDF format \(/download/relationship-between-attitude-motivation-and-workload-with-officers-performance-of-finding-leprosy-7835.pdf\)](#)
Abstract[Constraints in provision time of hospital medical record documents \(/article/constraints-in-provision-time-of-hospital-medical-record-documents-7836\)](#)

Ajeng Fauziah Kurniawati, Thinni Nurul Rochmah, Djazuly Chalidiyanto, Eka Nurul Hidayah Puspa Seruni

[Download Full Article - PDF format \(/download/constraints-in-provision-time-of-hospital-medical-record-documents-7836.pdf\)](#)
Abstract[Learning organization to maintain full accreditation of public health center \(/article/learning-organization-to-maintain-full-accreditation-of-public-health-center-7837\)](#)

Anna Wijayanti, Reinaldis Sara, Amalia Putri Handayani, Widy Tri Windy, Miftahul Sulaiman, Ratna Dwi Wulandari

[Download Full Article - PDF format \(/download/learning-organization-to-maintain-full-accreditation-of-public-health-center-7837.pdf\)](#)
Abstract[Implementation of lean management to reduce waiting time for drugs in Islamic Hospital, Surabaya \(/article/implementation-of-lean-management-to-reduce-waiting-time-for-drugs-in-islamic-hospital-surabaya-7838\)](#)

Halimah Salim Ahmad, Thinni Nurul Rochmah, Budhi Setianto

[Download Full Article - PDF format \(/download/implementation-of-lean-management-to-reduce-waiting-time-for-drugs-in-islamic-hospital-surabaya-7838.pdf\)](#)
Abstract[The effect of health education through brainstorming and booklet method on behavior in prevention of pulmonary Tb transmission \(/article/the-effect-of-health-education-through-brainstorming-and-booklet-method-on-behavior-in-prevention-of-7839\)](#)

Tintin Sukartini, Sri Kurniawati, Makhfudli Makhfudli

[Download Full Article - PDF format \(/download/the-effect-of-health-education-through-brainstorming-and-booklet-method-on-behavior-in-prevention-of-7839.pdf\)](#)
Abstract[Analysis of perceived health care quality on patient satisfaction \(/article/analysis-of-perceived-health-care-quality-on-patient-satisfaction-7840\)](#)

Ester Mariana, Wilda Apriyani, Stefanus Supriyanto

[Download Full Article - PDF format \(/download/analysis-of-perceived-health-care-quality-on-patient-satisfaction-7840.pdf\)](#) Abstract[Relationship between depression and stress with blood sugar levels in patients with diabetes melitus type II \(/article/relationship-between-depression-and-stress-with-blood-sugar-levels-in-patients-with-diabetes-melitus-7841\)](#)

Nurul Evriany, Galuh Nurul Fatimah, Djazuly Chalidiyanto

[Download Full Article - PDF format \(/download/relationship-between-depression-and-stress-with-blood-sugar-levels-in-patients-with-diabetes-melitus-7841.pdf\)](#)
Abstract[The analysis of stunting event factors in children aged 24-59 months based on transcultural nursing \(/article/the-analysis-of-stunting-event-factors-in-children-aged-24-59-months-based-on-transcultural-nursing-7842\)](#)

Esti Yunitasari, Nur Puji Winasis, Ira Suarilah

[Download Full Article - PDF format \(/download/the-analysis-of-stunting-event-factors-in-children-aged-24-59-months-based-on-transcultural-nursing-7842.pdf\)](#)
Abstract

[province-8128](#)

Haider Nadhim Abdaljabbar, Safa A. Faraj, Alaa Mohaisen AL-Rubae

[Download Full Article - PDF format \(/download/study-of-immune-thrombocytopenia-ito-in-iragis-children-in-wasit-province-8128.pdf\)](#)

Abstract

[Effect of the rutin on azathioprine-induced toxicity in reproductive function male rats \(/article/effect-of-the-rutin-on-azathioprine-induced-toxicity-in-reproductive-function-male-rats-8129\)](#)

Nassam Emad Daim, Hussein Khudair Al-Mayali

[Download Full Article - PDF format \(/download/effect-of-the-rutin-on-azathioprine-induced-toxicity-in-reproductive-function-male-rats-8129.pdf\)](#)

Abstract

[Investigation of interleukin 12 \(IL-12\) in graves' disease of Iraqi patients by using ELIZA \(/article/investigation-of-interleukin-12-il-12-in-graves-disease-of-iraqi-patients-by-using-eliza-8130\)](#)

Hind Suhail Ali, Hayfaa Mahmood Fahad, Mervit Bassim Jasim

[Download Full Article - PDF format \(/download/investigation-of-interleukin-12-il-12-in-graves-disease-of-iraqi-patients-by-using-eliza-8130.pdf\)](#)

Abstract

[A study to detect the most important virulence factors of cryptosporidium parasite samples by PCR \(/article/a-study-to-detect-the-most-important-virulence-factors-of-cryptosporidium-parasite-samples-by-pcr-8131\)](#)

Rana Saleh Al-Difaie, Nuha Qasim Mohammed, Khawla Hussien Sabbar

[Download Full Article - PDF format \(/download/a-study-to-detect-the-most-important-virulence-factors-of-cryptosporidium-parasite-samples-by-pcr-8131.pdf\)](#)

Abstract

[Effect of topical curcumin on the healing of major oral mucosal ulceration \(/article/effect-of-topical-curcumin-on-the-healing-of-major-oral-mucosal-ulceration-8132\)](#)

Muaid S. Abbas Shamash, Taghreed Fadhil Zaidan

[Download Full Article - PDF format \(/download/effect-of-topical-curcumin-on-the-healing-of-major-oral-mucosal-ulceration-8132.pdf\)](#)

Abstract

[Molecular detection of anaplasma marginale in ticks naturally feeding on cattle \(/article/molecular-detection-of-anaplasma-marginale-in-ticks-naturally-feeding-on-cattle-8133\)](#)

Aida H.H. Al-Obaidi, Gassan J.K. Al-Abedi, Estabraq A.N. Al-Zaidi

[Download Full Article - PDF format \(/download/molecular-detection-of-anaplasma-marginale-in-ticks-naturally-feeding-on-cattle-8133.pdf\)](#)

Abstract

[Expression of Bcl-2 protein and incidence of apoptosis of parietal layer epithelium cell glomerulus of kidneys in male rats \(Rattus norvegicus wistar\) on application of glutamin nephroprotective that are exposed to nephrotoxic modality of cisplatin chemotherapy \(/article/expression-of-bcl-2-protein-and-incidence-of-apoptosis-of-parietal-layer-epithelium-cell-glomerulus-8134\)](#)

Nur Wachid Yusuf, Imam Susilo, Tri Hartini Yuliawati, Miyayu Soneta Sofyan

[Download Full Article - PDF format \(/download/expression-of-bcl-2-protein-and-incidence-of-apoptosis-of-parietal-layer-epithelium-cell-glomerulus-8134.pdf\)](#)

Abstract

[Pelvic support osteotomy using ilizarov external fixator \(/article/pelvic-support-osteotomy-using-ilizarov-external-fixator-8135\)](#)

Ali Adel Mohammed Alsalihi, Mazin Ibrahim Khalel Thalaj

[Download Full Article - PDF format \(/download/pelvic-support-osteotomy-using-ilizarov-external-fixator-8135.pdf\)](#) Abstract[Studying the nutrition value and validity period of the processed product milk -like from chickpeas \(/article/studying-the-nutrition-value-and-validity-period-of-the-processed-product-milk-like-from-chickpeas-8136\)](#)

Ibtihal I. AL-Ani, Zaid A Thabit

[Download Full Article - PDF format \(/download/studying-the-nutrition-value-and-validity-period-of-the-processed-product-milk-like-from-chickpeas-8136.pdf\)](#)

Abstract



Expression of Bcl-2 protein and incidence of apoptosis of parietal layer epithelium cell glomerulus of kidneys in male rats (*Rattus norvegicus wistar*) on application of glutamin nephroprotective that are exposed to nephrotoxic modality of cisplatin chemotherapy

Nur Wachid Yusuf ¹, Imam Susilo ², Tri Hartini Yuliawati ³, Miyayu Soneta Sofyan ^{4*}

¹ Faculty of Medicine Universitas Airlangga, Surabaya, INDONESIA

² Department of Anatomic Pathology, Faculty of Medicine Universitas Airlangga, Surabaya, INDONESIA

³ Department of Histology and Anatomy, Faculty of Medicine Universitas Airlangga, Surabaya, INDONESIA

⁴ Department of health Faculty of Vocational Study Airlangga University, Surabaya, INDONESIA

*Corresponding author: miyayu@vokasi.unair.ac.id

Abstract

Cisplatin or (SP-4-2)-diamminedichloroplatinum (II) is one of the most potential platinum derivatives and is widely used for the treatment of various solid cancers such as testes, ovarian, head and neck, bladder, lung, and cervical cancers; melanoma; and lymphoma. The proapoptotic mechanism produced by cisplatin is quite effective in treating neoplastic cells. Cisplatin therapy is a non-target therapy. The cancer cell to which cisplatin is targeted inhibits several antiapoptotic regulators, so that cancer cells immediately start apoptosis. Increased apoptosis causes decreased Bcl-2 protein expression. This research is aimed at analyzing the effect of intravenous glutamine on the expression of Bcl-2 protein in the incidence of apoptosis in parietal layer epithelial cells of the glomerulus of male rats exposed to cisplatin. Glomerular epithelial cells are investigated as a marker of damage to the glomerulus. This study adopted an experimental design with "The Randomized Post Test Only Control Group Design" with a total sample size of 30 male rats that were randomly divided into three groups (randomized). Each group consisted of 10 male rats. Group P0 was a control without any injection, only standard diet; P1 group was injected intraperitoneally with a dose of 20 mg/kg of cisplatin on seventh day; and group P2 was injected intravenously with a dose of 100 mg/kgBW of glutamine for seven days then injected intraperitoneally with 20 mg/kg of cisplatin on seventh day. There was no significant effect but moderate correlation change with $p > 0.05$ administration of intravenous glutamine on the expression of Bcl-2 proteins in the parietal layer epithelial cell glomerulus the incidence of apoptosis male rats exposed to cisplatin.

Keywords: glutamine, Bcl-2, apoptosis, cisplatin

Yusuf NW, Susilo I, Yuliawati TH, Sofyan MS (2020) Expression of Bcl-2 protein and incidence of apoptosis of parietal layer epithelium cell glomerulus of kidneys in male rats (*Rattus norvegicus wistar*) on application of glutamin nephroprotective that are exposed to nephrotoxic modality of cisplatin chemotherapy. Eurasia J Biosci 14: 4667-4671.

© 2020 Yusuf et al.

This is an open-access article distributed under the terms of the Creative Commons Attribution License.

INTRODUCTION

The kidney is a filtration organ in humans that functions to filter and remove metabolic waste products out through urine. This organ is divided into four compartments namely Bowman capsule, essence, tubules, and blood vessels (Yang et al., 2016). The Bowman capsule compartment contains the glomerulus which contains afferent and efferent blood vessels. In the inner vessel wall, there is a layer of endothelial cells that play a role in supporting the glomerular filtration function. On the glomerular outer wall, there is a visceral epithelial layer consisting of podocyte cells and parietal

epithelium attached to the inner wall of the Bowman capsule (Yang et al., 2016).

In cases of acute or chronic kidney failure, the glomerulus filtration rate decreases; this is one of the reasons for damage to glomerular endothelial cells accompanied by damage to the visceral and parietal epithelial lining. The glomerular filtration rate (GFR) can be calculated by measuring creatinine levels in urine. The higher the creatinine level, the lower the filtration

Received: May 2019

Accepted: April 2020

Printed: October 2020

rate. Therefore, high creatinine levels can be used as an indication of kidney failure (Bastard et al., 2019).

The number of patients with chronic kidney failure in Indonesia tended to show an increase of 1.8 per ml from 2013 to 2018 (Balitbangkes, 2018). This increase indicates that the kidney is an organ that is prone to neoplastic and non-neoplastic damage. Neoplastic causes can be observed from kidney malignancies such as renal cell carcinoma, including clear cell carcinoma, papillary renal cell carcinoma, and chromophobe renal cell carcinoma (Verratti et al., 2019). By contrast, non-neoplastic damage is seen from damage to filtration function without malignancies, such as renal failure due to hypertension (Judd and Calhoun, 2015), diabetes mellitus (Karner-Hutuleac, 2012), and nephrotoxic effects of drugs (Qu et al., 2018). One nephrotoxic effect arises from the use of long-term chemotherapy (Alibakhshi et al., 2018).

Nephrotoxic prevalence in the use of chemotherapy for bone cancer treatment shows a diagnosis of bone metastasis; the average age is 67 years, and 24% of the patients show renal insufficiency (RI). The 5-year prevalence is 43% for RI and 71% for chronic kidney disease (CKD) among RI patients. Nearly half (46%) of CKD patients received intravenous bisphosphonate (IV BP) within 12 months after eGFR confirmation, and 13% of these patients received at least one other nephrotoxic agent during that period (Hernandez et al., 2015). In Indonesia, the prevalence is 34.1% of patients experiencing nephrotoxic effects from cisplatin chemotherapy (Prasaja et al., 2015).

One of the chemotherapy materials used is cisplatin. Its wide use in benign and malignant neoplasms makes it the first choice in cancer therapy. However, recent research demonstrates that cisplatin causes damage to tubular epithelial cells and glomerulus. Cisplatin causes apoptosis in neoplastic cells, but normal cells can be affected by similar apoptosis (Gómez-Sierra et al., 2018).

The increase in the incidence of apoptosis in normal cells can be evaluated with proapoptotic and antiapoptotic proteins. Commonly known proapoptotic markers are Bcl-2-associated x protein (Bax), cysteine-aspartate protease (caspase 12), Apaf-1, and procaspase 9, whereas antiapoptotic proteins such as Bcl-2 (Portt et al., 2011). Decreased expression of the Bcl-2 protein from the normal threshold in the administration of chemotherapy shows that there has been damage to the epithelial cells of the glomerular visceral and parietal layers. Examination of Bcl-2 protein expression is done through immunohistochemical staining with the Bcl-2 antigen (Portt et al., 2011). Nephrotoxic effects above are needed materials that can reduce the level of damage called nephroprotective substances. These materials can be synthesized chemically or from natural materials such as glutamine, zingerone, L-theanine, and virgin coconut oil (Alibakhshi

et al., 2018, Altıkkaynak et al., 2018, Famurewa et al., 2017).

From the description above, the use of chemotherapy cannot be avoided causing damage to the kidneys. Thus, cancer patients who get chemotherapy are at risk of chronic kidney failure. Then, further research is needed on the right combination of therapies for chemotherapy and nephroprotective substances so that nephrotoxic side effects can be suppressed. Glutamine is a solution that is being developed because it inhibits the nephrotoxic effects of cisplatin by inhibiting OCT2 receptors, p53 protein, caspase 3, and TNF- α . The combination of glutamine with cisplatin is likely to increase the efficacy and safety of chemotherapy. It is expected that with the use of glutamine as a nephroprotective agent, patients who receive chemotherapy can avoid the risk of damage to the kidneys (Gao et al., 2019).

MATERIALS AND METHODS

Animal and treatments

White rat (*Rattus norvegicus*) strain of male Wistar obtained from the experimental animal unit of the Faculty of Medicine, Airlangga University, which related the inclusion and exclusion criteria. Rats are placed in a cage with one cage containing one mouse. Rat food in the form of standard rat food pellets is given *ad libitum*, and drinks in the form of bottled water are given *ad libitum*.

Chemicals

Glutamine solution was prepared with a dose of 1 g of glutamine diluted in 10 ml of PZ solution. Glutamine is given intravenously to rat tails at a dose of 100 mg/kgBB daily for 6 consecutive days. Cisplatin is given intraperitoneally with a single dose of 20 mg/kgBW Apoptotic Detection Kit POD (11684817910 ROCHE), anti-Bcl-2 antibodies (Santa Cruz).

Experimental design

Wistar strain male white rats amounted to 30 at the start of the study divided into three groups randomly; the control group (P0) was sacrificed by cervical dislocation after anesthesia with ether. Then, the kidney organs were taken for the preparation of immunohistochemistry.

Group P1 was given a single dose of intraperitoneal cisplatin injection of 20 mg/kgBW on day 7 and then observed for 72 hours. Then, the rats were sacrificed on the 10th day by cervical dislocation after ether anesthesia; then, the kidney was taken for the preparation of immunohistochemistry. P2 groups from day 1 to day 7 were given intravenous injection of glutamine at a dose of 100 mg/kgBW once a day, and on day, seven mice were given a single dose of intraperitoneal injection of 20 mg/kgBW cisplatin. Then, the rats were observed for 72 hours and then sacrificed on the 10th day by means of cervical dislocation after anesthesia with ether; then, the kidney organs were

taken for making immunohistochemical preparations. The observation time on the 10th day after cisplatin injection was apoptotic in parietal capsula Bowman epithelial cells (Tsuruya et al. 2003).

Histopathological preparation

On the 10th day, rats in groups P0, P1, and P2 were killed by cervical dislocation after anesthesia with ether, and abdominal dissection of the rats was performed to remove the kidney.

Kidney tissue is fixed to 10% formalin for 15–24 hours. After that, dehydration is done using multilevel alcohol to prevent tissue morphology changes (30%, 50%, 70%, 80%, 96%, and absolute) for 60 minutes, successively. Clearing was done using xylol twice every 60 minutes. Then, infiltration with soft paraffin was carried out for 60 minutes at a temperature of 48 degrees.

Then, a block was formed in hard paraffin on the mold and allowed to stand for a day. The next day, it was placed on the holder and cut 4–5 μm thick with a rotary microtome. After that, the object glass was mounted with poly-L-lysine coated. The glass of the object produced by paraffin block was immersed in xylol for 5 minutes twice. After that, rehydration was done using gradual alcohol (absolute, 96%, 80%, 70%, 50%, and 30%) for 5 minutes. Then, sample was rinsed in dH₂O for 5 minutes.

Immunohistochemistry assay Bcl-2

The slides were washed using PBS pH 7.4 once for 5 minutes. Thereafter was endogenous peroxide blocking used 3% H₂O₂ for 20 minutes. Washed using PBS pH 7.4 three times, each for 5 minutes. Unspecific protein blocking used 5% FBS containing 0.25% Triton X-100. Washed using PBS pH 7.4 three times, each for 5 minutes. Incubation using primary antibodies (monoclonal anti-Bcl-2) 60 minute at 25°C. Washed using PBS pH 7.4 three times, each for 5 minutes. Incubation using an anti-mouse biotin conjugated antibody for 20 minutes at room temperature. Washed using PBS pH 7.4 three times, each for 5 minutes. Incubation used SA-HRP (Strep-Avidin Horse Radix Peroxidase) for 40 minutes. Washed using PBS pH 7.4 three times, each for 5 minutes. Drops with diaminobenzidine and incubation for 3 minutes. Washed using PBS pH 7.4 three times, each for 5 minutes. Counterstaining using Mayer Hematoxylin incubated for 10 minutes and washing using tap water. Rinsed using dH₂O and air-dried. The mounting was done using the lid and cover with a glass cover. Looked under a light microscope at 400 \times magnification.

Actually, there is similarity between the IHC process for Bcl-2 protein and caspase 12; the difference is only in the incubation period of primary antibodies. Caspase 2 needed 24 hours, and Bcl-2 only needed 60 minutes. The first or primary antibody will be shown in brown and blue for a cell that is not shown in Bcl-2. The glomerular

Table 1. Descriptive statistic of express Bcl-2 protein and apoptotic cell

Variable	Glomerular epithelial expressing Bcl-2 protein	Apoptotic cell
	Average \pm SD	Average \pm SD
P0	5.3 \pm 0.71	23.1 \pm 3.3
P1	6.4 \pm 0.37	28.1 \pm 4.3
P2	6.3 \pm 0.21	27.2 \pm 4.05

Table 2. Mann-Whitney U test for the Bcl-2 protein between P0 and P1 group

Test	Score
Mann-Whitney U	5.000
Wilcoxon W	60.000
Z	-3.411
Asymp. Sig. (two-tailed)	0.001
Exact Sig. [2*(one-tailed sig.)]	0.000 ^b

Table 3. Mann-Whitney U test for the Bcl-2 protein between P1 and P2 group

Test	Score
Mann-Whitney U	48.000
Wilcoxon W	103.000
Z	-0.154
Asymp. Sig. (two-tailed)	0.878
Exact Sig. [2*(one-tailed sig.)]	0.912 ^b

epithelial cells was counted in teen place in every slide: three in the upper pole, four in the middle pole, and three in the lower pole.

Statistical analysis

All dependent variables used in this study are variables with a ratio data scale, so it is necessary to do a normality test with the Shapiro-Wilk test ($\alpha = 0.05$) and homogeneity test with the Levene test ($\alpha = 0.05$). If the normality test results show a normal distribution, then a different test with ANOVA ($\alpha = 0.05$), and if there are differences followed by the *least significant difference* (LSD) ($\alpha = 0.05$). If the results of the normality test show an abnormal and homogeneous or normal and non-homogeneous distribution, then a different test is performed with the Kruskal–Wallis test ($\alpha = 0.05$), and if there is a difference then followed by the T-independent test or the Mann–Whitney test ($\alpha = 0.05$).

RESULTS

Immunohistochemical examination results of rats with Bcl-2 antibodies showed changes in expression in each group based on descriptive statistic Bcl-2 expression and apoptotic cells in each group (**Table 1**).

Group P0 is a control group without any injection, only standard dietary; P1 group was given intraperitoneal injection of a single dose of 20 mg/kg cisplatin on the seventh day; and group P2 was given an injection of 100 mg/KgBW glutamine intravenous on days 1–7 and an intraperitoneal injection of a single dose of cisplatin 20 mg/kg on the seventh day.

There was a difference in P0 and P1 group of expression of the Bcl-2 protein, following the Mann–Whitney U test. Difference will be stated if Asymp. Sig < 0.05 (**Table 2**). Meanwhile, P1 and P2 did not have a difference because Asymp. Sig > 0.05 (**Table 3**).

Table 4. Pearson correlation analysis results

		Score	Group
Score	Pearson's correlation	1	0.428
	Sig. (two-tailed)		0.021
	N	30	29
Group	Pearson's correlation	0.428*	1
	Sig. (two-tailed)	0.021	
	N	29	29

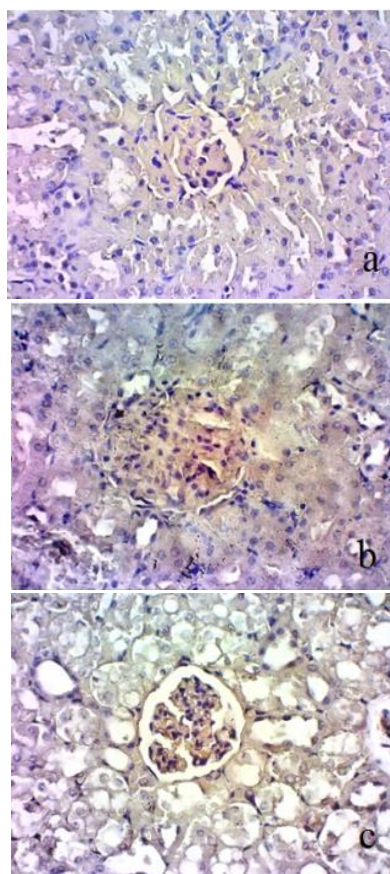


Fig. 1. IHC with the Bcl-2 protein. (a) group P0 as the control group, without any injection, only standard dietary; (b) P1 group was given intraperitoneal injection of a single dose of 20 mg/kg cisplatin on the seventh day; and (c) group P2 was given an injection of 100 mg/KgBW glutamine intravenous on days 1–7 and an intraperitoneal injection of a single dose of cisplatin 20 mg/kg on the seventh day

For the apoptotic cell, have same result for expressed Bcl-2 protein, following the Mann–Whitney U test. This indicated a difference between the P0 and P1 groups but no difference for P1 and P2. However, it still has moderate correlation among Bcl-2 expressed in normal cell and the apoptotic cell. This is shown by Pearson's correlation analysis (Table 4).

The results obtained indicated that there was a change in the expression of the Bcl-2 protein and

apoptosis that occurred between the P0 group as a control and P1 with the treatment of a single dose of intraperitoneal injection of 20 mg/kg cisplatin administration. In the P1 group (administration of a single dose of intraperitoneal injection of 20 mg/kg cisplatin) and P2 (treatment of intravenous injection of 100 mg/kgW glutamine for 7 days and a single dose of cisplatin), there were no significant expression changes, but still any changes each group (Fig. 1).

DISCUSSION

Cisplatin enters the cytoplasm cell by passing through the OCT2 receptor. These receptors are sensitive to cisplatin stimulation, so that if the amount of cisplatin outside the cell increases, the number of these receptors will also increase. An increase in the number of receptors will transport large amounts of cisplatin into the cell and induce apoptosis (Filipski et al., 2009). In P0 and P1, there are significant changes according to the Mann–Whitney U test. These changes are triggered because cisplatin entering the normal cell induces apoptosis.

This is supported by Pearson's correlation test for the number of Bcl-2 expressions, which are antiapoptotic markers with an increasing number of apoptotic cells. Bcl-2 in normal cells is limited in production to keep cells alive according to their time. However, when starting apoptosis induced by cisplatin, the expression will be suppressed by the p53 protein. If glutamine is present, the OCT2 receptor number will be reduced so that the amount of cisplatin that enters the cell is reduced (Kim et al., 2015). The Pearson correlation test indicates that this occurs at P0 and P1, but it is not highly correlated with P2.

Glutamine works by inhibiting the expression and activation of p53 protein, caspase 3, and OCT2 receptors. Glutamine reduces the effects of cisplatin slightly, as evidenced by the decrease in apoptosis with Bcl-2 expression still above normal, even close to the P1 value. Basically, the production of Bcl-2 will be increased if the cell is exposed to damaging substances, with the aim that the cell will survive like a carcinoma cell (Kim et al., 2015).

CONCLUSION

Glutamine can little decrease the expression of Bcl-2 proteins and decrease apoptosis of parietal layer epithelium cell of glomerulus of kidneys male rats exposed cisplatin.

REFERENCES

- Alibakhshi, T. Khodayar MJ, Khorsandi L, Rashno M, Zeidooni L. (2018) 'Protective effects of zingerone on oxidative stress and inflammation in cisplatin-induced rat nephrotoxicity', *Biomedicine and Pharmacotherapy*, 105(March), pp. 225–232. doi: 10.1016/j.biopha.2018.05.085.

- Altinkaynak, Y, Kural B, Akcan BA, Bodur A, Özer S, Yuluğ E, et al. et al. (2018) 'Protective effects of L-theanine against doxorubicin-induced nephrotoxicity in rats', *Biomedicine and Pharmacotherapy*, 108(September), pp. 1524–1534. doi: 10.1016/j.biopha.2018.09.171.
- Balitbangkes. (2019) Laporan Nasional Rischesdas 2018. Jakarta: Balitbangkes p.169
- Bastard, J. P. Fellahi S, Regeniter A, Capeau J, Ronco P, Plaisier E. (2019) 'Aside from acute renal failure cases, are urinary markers of glomerular and tubular function useful in clinical practice?', *Clinical Biochemistry*. Elsevier, 65(June 2018), pp. 1–6. doi: 10.1016/j.clinbiochem.2019.01.006.
- Famurewa, A. C. Aja PM, Maduagwuna EK, Ekeleme-Egedigwe CA, Ufebe OG, Azubuike-Osu SO. (2017) 'Antioxidant and anti-inflammatory effects of virgin coconut oil supplementation abrogate acute chemotherapy oxidative nephrotoxicity induced by anticancer drug methotrexate in rats', *Biomedicine and Pharmacotherapy*. Elsevier, 96(December), pp. 905–911. doi: 10.1016/j.biopha.2017.12.008.
- Filipski, K., Mathijssen, R., Mikkelsen, T. et al. (2009). Contribution of Organic Cation Transporter 2 (OCT2) to Cisplatin-Induced Nephrotoxicity. *Clinical Pharmacology & Therapeutics*, [online] 86(4), pp.396-402.
- Gao, H, Zhang S, Hu T, Qu X, Zhai J, Zhang Y, et al. (2019) 'Omeprazole protects against cisplatin-induced nephrotoxicity by alleviating oxidative stress, inflammation, and transporter-mediated cisplatin accumulation in rats and HK-2 cells', *Chemico-Biological Interactions*. Elsevier, 297(June 2018), pp. 130–140. doi: 10.1016/j.cbi.2018.11.008.
- Ghosh, S. (2019). Cisplatin: The first metal based anticancer drug. *Bioorganic Chemistry*, 88, p.102925.
- Gómez-Sierra, T, Eugenio-Pérez D, Sánchez-Chinchillas A, Pedraza-Chaverri J. (2018) 'Role of food-derived antioxidants against cisplatin induced-nephrotoxicity', *Food and Chemical Toxicology*. Pergamon, 120, pp. 230–242. doi: 10.1016/J.FCT.2018.07.018.
- Hernandez RK, Adhia A, Wade SW, O'Connor E, Arellano J, Francis K, et al (2015). Prevalence of bone metastases and bone-targeting agent use among solid tumor patients in the United States. *Clin Epidemiol.*;7:335–45.
- Judd, E. and Calhoun, D. A. (2015) 'Management of hypertension in CKD: beyond the guidelines', *Advances in chronic kidney disease*, 22(2), pp. 116–122. doi: 10.1053/j.ackd.2014.12.001.
- Karner-Hutuleac, A. (2012) 'Health related quality of life of diabetic and chronic renal failure patients', *Procedia - Social and Behavioral Sciences*. Elsevier, 33, pp. 85–89. doi: 10.1016/J.SBSPRO.2012.01.088.
- Kim, H. J, Park DJ, Kim JH, Jeong EY, Jung MH, Kim TH, et al. (2015) 'Glutamine protects against cisplatin-induced nephrotoxicity by decreasing cisplatin accumulation', *Journal of Pharmacological Sciences*. Elsevier Ltd, 127(1), pp. 117–126. doi: 10.1016/j.jphs.2014.11.009.
- Portt, L, Norman G, Clapp C, Greenwood M, Greenwood MT. (2011) 'Anti-apoptosis and cell survival: A review', *Biochimica et Biophysica Acta - Molecular Cell Research*. Elsevier B.V., 1813(1), pp. 238–259. doi: 10.1016/j.bbamcr.2010.10.010.
- Prasaja, Y., Sutandyo, N. and Andrajati, R. (2015) "Incidence of Cisplatin-Induced Nephrotoxicity and Associated Factors among Cancer Patients in Indonesia," *Asian Pacific Journal of Cancer Prevention*. Asian Pacific Organization for Cancer Prevention, 16(3), pp. 1117–1122. doi: 10.7314/apjcp.2015.16.3.1117.
- Quintanilha, Saavedra KF, Visacri MB, Moriel P, Salazar LA. (2019) 'Role of epigenetic mechanisms in cisplatin-induced toxicity', *Critical Reviews in Oncology/Hematology*. Elsevier, 137(August 2018), pp. 131–142. doi: 10.1016/j.critrevonc.2019.03.004.
- Tsuruya, K, Ninomiya, T, & Tokumoto, M 2003, Direct Involvement of The Receptor-mediated Apoptotic Pathways in Cisplatin-induced Renal Tubular Cell Death, *Kidney Int*, vol 63, pp 72-82
- Verratti, V, Brunetti L, Ferrante C, Orlando G, Recinella L, Chiavaroli A, et al. (2019) 'Physiological and pathological levels of prostaglandin E2 in renal parenchyma and neoplastic renal tissue', *Prostaglandins & Other Lipid Mediators*. Elsevier, 141, pp. 11–13. doi: 10.1016/J.PROSTAGLANDINS.2019.02.004.
- Yang, X, Le Minh H, (Tim) Cheng K-T, Sung KH, Liu W. (2016) 'Renal compartment segmentation in DCE-MRI images', *Medical Image Analysis*. Elsevier, 32, pp. 269–280. doi: 10.1016/J.MEDIA.2016.05.006.